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**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A SUBMISSION UNDER 35 U.S.C. 371**

ATTORNEY'S DOCKET NUMBER

05313/HG

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

10/535,000

PRIORITY DATE CLAIMED

18 November 2002

INTERNATIONAL APPLICATION NO.

PCT/JP03/14559

INTERNATIONAL FILING DATE

17 November 2003

TITLE OF INVENTION

Therapeutic Agent for Glaucoma Comprising Rho Kinase Inhibitor,
and β -Blocker

APPLICANT(S) FOR DO/EO/US

Masakazu HATANO; Tadashi NAKAJIMA; Takeshi MATSUGI; Hideaki HARA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☐ This is a **FIRST** submission of items concerning a submission under 35 U.S.C. 371.
2. ☒ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a submission under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected (Article 31).
5. ☐ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☐ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

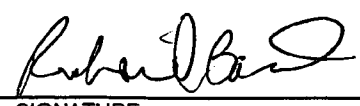
Items 11 to 20 below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A preliminary amendment.
14. ☐ An Application Data Sheet under 37 CFR 1.76.
15. ☐ A substitute specification.
16. ☐ A change of correspondence address letter (Form PTO/SB/122).
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.
18. ☐ A second copy of the published International Application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☐ Other items or information:

Express Mail Label No. EV 704 327 912 US
Date of Deposit: June 27, 2005

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above with sufficient postage, and is addressed to the Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450

Dorothy DeFrancesco
Dorothy DeFrancesco

| | | | | | |
|--|--------------|---|--|--------------------------|-------------------|
| U.S. APPLICATION NO. (if known, 37 CFR 1.5) | | INTERNATIONAL APPLICATION NO. | | ATTORNEY'S DOCKET NUMBER | |
| 10/535,000 | | PCT/JP03/14559 | | 05318/HG | |
| 21. The following fees are submitted: | | | | | |
| <input checked="" type="checkbox"/> a) Basic national fee..... | | | | \$300.00 | \$ 300.00 |
| <input checked="" type="checkbox"/> b) Examination fee..... | | | | \$200.00 | \$ 200.00 |
| <input checked="" type="checkbox"/> c) Search fee..... | | | | \$500.00 | \$ 500.00 |
| TOTAL OF ABOVE CALCULATIONS = | | | | \$1000.00 | \$ 1000.00 |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof. | | | | | |
| Total Sheets | Extra sheets | Number of each additional 50 or fraction thereof (round up to a whole number) | RATE | | |
| - 100 = | /50 = | | x \$250.00 | \$ | .00 |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)). | | | | \$ | .00 |
| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE | \$ | |
| Total claims | - 20 = | | x \$50.00 | \$ | .00 |
| Independent claims | - 3 = | | x \$200.00 | \$ | .00 |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | + \$360.00 | \$ | .00 |
| TOTAL OF ABOVE CALCULATIONS = | | | | \$ | .00 |
| <input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. | | | | \$ | .00 |
| SUBTOTAL = | | | | \$ | .00 |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | | + | \$.00 |
| TOTAL NATIONAL FEE = | | | | \$ | .00 |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property | | | | + | \$.00 |
| TOTAL FEES ENCLOSED = | | | | \$ | .00 |
| | | | | Amount to be refunded: | \$.00 |
| | | | | Amount to be charged: | \$.00 |
| a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed. | | | | | |
| b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. | | | | | |
| c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>06-1378</u> . A duplicate copy of this sheet is enclosed. | | | | | |
| d. <input type="checkbox"/> Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038. | | | | | |
| NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the International Application to pending status. | | | | | |
| SEND ALL CORRESPONDENCE TO: | | | | | |
| CUSTOMER NO. 01933 | | |  | | |
| Richard S. Barth, Esq. | | | SIGNATURE | | |
| Frishauf, Holtz, Goodman & Chick, PC | | | Richard S. Barth | | |
| 220 Fifth Ave. - 16th Floor | | | NAME | | |
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**IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE**

Serial No. : 10/535,000
Applicants : Masakazu HATANO et al.
Filed : May 16, 2005
For : THERAPEUTIC AGENT FOR
GLAUCOMA COMPRISING Rho
KINASE INHIBITOR AND
 β -BLOCKER
Docket No. : 05318/HG
Customer No.: 01933

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

MAIL STOP PCT

S I R :

The above-identified application is a U.S. national phase application of PCT/JP03/14559.

This INFORMATION DISCLOSURE STATEMENT ("IDS") serves to supplement the IDS filed on May 16, 2005.

Submitted herewith are the following:

(1) copy of the International Search Report for
PCT/JP03/14559;

(2) copies of the publications cited in said International Search Report and on page 2 of the present specification; and

Express Mail Mailing Label
No.: EV 704 327 912 US
Date of Deposit: June 27, 2005
I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 with sufficient postage on the date indicated above and is addressed to:
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Commissioner for Patents.
P.O. Box 1450
Alexandria, VA 22313-1450

Dorothy DeFrancesco
Dorothy DeFrancesco

In the event that this Paper is late filed, and the necessary petition for extension of time is not filed concurrently herewith, please consider this as a Petition for the requisite extension of time, and to the extent not tendered by check attached hereto, authorization to charge the extension fee, or any other fee required in connection with this Paper to Account No. 06-1378.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /G.H./

(3) Forms PTO/SB/08A and PTO/SB/08B.

It is respectfully requested that initialed copies of the Forms PTO/SB/08A and PTO/SB/08B be returned to the undersigned to indicate that the publications listed therein have been considered and made of record.

Respectfully submitted,



RICHARD S. BARTH
REG. NO. 28,180

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RSB/ddf

Encs.: (1) Copy of International Search Report
for PCT/JP03/14559
(2) Forms PTO/SB/08A and PTO/SB/08B
(3) copies of publications listed
in said Forms PTO/SB/08A and PTO/SB/08B

Please type a plus sign (+) inside this box →



Rec'd PCT/PTO 27 JUN 2005

PTO/SB/08A (08-00)

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

| | | | | | | | |
|---|---|----|---|------------------------|--|-----------------|--|
| Substitute for Form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT | | | | Application Number | | 10/535,000 | |
| | | | | Filed | | May 16, 2005 | |
| | | | | First Named Inventor | | Masakazu HATANO | |
| | | | | Group Art Unit | | | |
| | | | | Examiner Name | | | |
| Sheet | 1 | of | 2 | Attorney Docket Number | | 05318/HG | |

U.S. PATENT DOCUMENTS

| Exam. Inits [*] | Cite No ¹ | Document Number | Kind Code ² | Name of Patentee or Applicant | Publication Date MM-DD-YYYY | Relevant Portion |
|--------------------------|----------------------|-----------------|------------------------|-------------------------------|-----------------------------|------------------|
| | | | | | | |

FOREIGN PATENT DOCUMENTS

| Exam. Inits [*] | Cite No ¹ | Office ³ | Document Number ⁴ | Kind Code ⁵ | Name of Patentee or Applicant | Publication Date MM-DD-YYYY | Relevant Portion | T ⁶ |
|--------------------------|----------------------|---------------------|------------------------------|------------------------|---|-----------------------------|------------------|----------------|
| | | EP | 1034793 | A1 | Senju Pharmaceutical Co., Ltd. et al. | 09-13-2000 | | |
| | | EP | 956865 | A1 | Yoshitomi Pharmaceutical Industries, Ltd. | 11-17-1999 | | |
| | | EP | 286903 | A1 | The Trustees of Columbia University | 10-19-1988 | | |
| | | WO | 97/23222 | A1 | Alcon Laboratories, Inc. | 07-03-1997 | | |
| | | WO | 02/38158 | A1 | Pharmacia AB | 05-16-2002 | | |
| | | WO | 93/16701 | A2 | Alcon Laboratories, Inc. | 09-02-1993 | | |
| | | WO | 03/049745 | A1 | Pharmacia Corp. | 06-19-2003 | | |
| | | WO | 00/09162 | A1 | Senju Pharmaceutical Co., Ltd. et al. | 02-24-2000 | | * |
| | | JP | 2726672 | B2 | | 12-05-1997 | | |

not considered
no translation

| | | | |
|--------------------|--------------|-----------------|------------|
| Examiner Signature | /Gigi Huang/ | Date Considered | 05/12/2009 |
|--------------------|--------------|-----------------|------------|

* EXAMINER: Initial if document considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Place a check here if English translation is attached.

DATE MAILED: JUNE 27, 2005

*WO 00/09162 IS A FAMILY MEMBER OF EP 1034793

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| | | | | | |
|---|--------------------------|--|---|------------------------|-----------------|
| Substitute for Form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT | | | | Application Number | 10/535,000 |
| | | | | Filing Date | MAY 16, 2005 |
| | | | | First Named Inventor | Masakazu HATANO |
| | | | | Group Art Unit | |
| | | | | Examiner Name | |
| Sheet | 2 | of | 2 | Attorney Docket Number | 05318/HG |
| OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS | | | | | |
| Examiner Initials ¹ | Cite No. ¹ | Include name of author (in CAPITAL LETTERS), title of article, title of item, date, page(s), volume-issue number(s), publisher, city and/or country where published | | | T ² |
| | | UEHARA, M. et al., "Calcium Sensitization of Smooth Muscle Mediated by a Rho-Associated Protein Kinase in Hypertension," <u>Nature</u> , (1997), <u>389</u> , pp. 990 to 994. Mariko ASahi et al., "Ryokunaisho to Ryokunaisho Chiryo Yakuzai (Fukuyaki Shido Manual II, Dai 10 Kai)," <u>The Pharmaceuticals Monthly</u> , (1996), <u>38(9)</u> , pp. 2311 to 2331. Kunitaru SHIRATO, "I. Ryokunaisho no Yakubutsu Ryoho 1. Gairon" (Chiryoyaku no Sentaku o Dou Kangaerunoka), ("Some Practical Aspect in Medical Therapy") Ganka, (2002), <u>44(11)</u> , pp. 1443 to 1448. Tatsuro FUKUCHI, "I. Ryokunaisho no Yakubutsu Ryoho 2. Ryokunaisho Chiryoyaku C. Kokan Shinkei Sogaiyaku β Shadanyaku," ("β-Adrenergic Antagonists") Ganka, (2002), <u>44(11)</u> , pp. 1458 to 1463. Ikuo AZUMA et al., "Effects of Bunazosin Hydrochloride Ophthalmic Solution in Combination with Timolol Maleate Ophthalmic Solution in Patients with Open-Angle Glaucoma and Ocular Hypertension-Comparison with Dipivefrin Hydrochloride Ophthalmic Solution," <u>The Journal of the Eye</u> , (2002), <u>19(2)</u> , pp. 261 to 266. Yuichiro OTAKE et al., "Effect and Safety of Combined Therapy with Betaxolol and isopropyl Unoprostone," <u>The Journal of the Eye</u> , (2000), <u>17(5)</u> , pp. 687 to 690. Hideki TOKUSHIGE, "ROCK Sogaiyaku to Ryokunaisho" ("ROCK Inhibitor and Glaucoma"), <u>BIO Clinica</u> , (2002), <u>17(13)</u> , pp. 1191 to 1194. HOYNG, P.F.J. et al., "Pharmacological Therapy for Glaucoma," <u>Drugs</u> , (2000), <u>59(3)</u> , pp. 411 to 434. Megumi HONJO et al., "Effects of Rho-Associated Protein Kinase Inhibitor Y-27632 on Intraocular Pressure and Outflow Facility," <u>Invest. Ophthalmol. & Vis. Sci.</u> , Vol. 42, No. 1 (2001), pp. 137-144. P. Vasantha RAO et al., "Modulation of Aqueous Humor Outflow Facility by the Rho Kinase-Specific Inhibitor Y-27632," <u>Invest. Ophthalmol. & Vis. Sci.</u> , Vol. 42, No. 5 (2001), pp. 1029-1037. | | | |
| Examiner Signature | /Gigi Huang/ | | | Date Considered | 05/12/2009 |

* EXAMINER: Initial if document considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² Place a check here if English translation is attached.

DATE MAILED: JUNE 27, 2005

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /G.H./